```
=> FIL MEDLINE BIOSIS CA EMBASE SCISEARCH
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.26       1.26

FILE 'MEDLINE' ENTERED AT 14:14:16 ON 18 AUG 2006

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FILE 'CA' ENTERED AT 14:14:16 ON 18 AUG 2006
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FILE 'SCISEARCH' ENTERED AT 14:14:16 ON 18 AUG 2006
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=> s mnsod or ((manganese or mn) (n) (sod or sod# or (superoxide dismutase#)))
L1        20334 MNSOD OR ((MANGANESE OR MN) (N) (SOD OR SOD# OR (SUPEROXIDE
                DISMUTASE#)))

=> s antisense or anti-sense or (comple? (2n) (oligonucl? or nucle?))
   3 FILES SEARCHED...
L2       259138 ANTISENSE OR ANTI-SENSE OR (COMPLE? (2N) (OLIGONUCL? OR NUCLE?))


=> s l1 and l2
L3          487 L1 AND L2

=> s l1 (p) l2
L4          450 L1 (P) L2

=> s l1 (5n) l2
L5          258 L1 (5N) L2

=> s l5 and py<=2000
   1 FILES SEARCHED...
L6          129 L5 AND PY<=2000

=> s l6 and start codon
L7            0 L6 AND START CODON

=> s l6 and (human (s) l1)
L8           67 L6 AND (HUMAN (S) L1)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           26 DUP REM L8 (41 DUPLICATES REMOVED)

=> s l6 and codon
L10           0 L6 AND CODON

=> s l6 and start
L11           0 L6 AND START

=> s OBERLEY, L?/au;s WEYDERT, C?/au;s SMITH, B?/au
L12        1364 OBERLEY, L?/AU
```

```
L13         117 WEYDERT, C?/AU


S SMITH, IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s SMITH, B?/au
S SMITH, IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s SMITH, B?/au
L14       26888 SMITH, B?/AU

=> s l12 or l13 or l14
L15       28248 L12 OR L13 OR L14

=> d his

     (FILE 'HOME' ENTERED AT 14:11:01 ON 18 AUG 2006)

     FILE 'MEDLINE, BIOSIS, CA, EMBASE, SCISEARCH' ENTERED AT 14:14:16 ON 18
     AUG 2006
L1         20334 S MNSOD OR ((MANGANESE OR MN) (N) (SOD OR SOD# OR (SUPEROXIDE D
L2        259138 S ANTISENSE OR ANTI-SENSE OR (COMPLE? (2N) (OLIGONUCL? OR NUCLE
L3           487 S L1 AND L2
L4           450 S L1 (P) L2
L5           258 S L1 (5N) L2
L6           129 S L5 AND PY<=2000
L7             0 S L6 AND START CODON
L8            67 S L6 AND (HUMAN (S) L1)
L9            26 DUP REM L8 (41 DUPLICATES REMOVED)
L10            0 S L6 AND CODON
L11            0 S L6 AND START
L12         1364 S OBERLEY, L?/AU
L13          117 S WEYDERT, C?/AU
L14        26888 S SMITH, B?/AU
L15        28248 S L12 OR L13 OR L14

=> s l15 and l1
L16          635 L15 AND L1

=> s l13 or l14
L17       26999 L13 OR L14

=> s l13 or l12
L18        1376 L13 OR L12

=> s l18 and l1
L19          635 L18 AND L1

=> s l19 and l2
L20           31 L19 AND L2

=> dup rem l20
PROCESSING COMPLETED FOR L20
L21            9 DUP REM L20 (22 DUPLICATES REMOVED)

=> s l21 or l9
L22           31 L21 OR L9
```

=> dup rem l22
PROCESSING COMPLETED FOR L22
L23 31 DUP REM L22 (0 DUPLICATES REMOVED)

=> d l23 ibib abs 1-31

L23 ANSWER 1 OF 31 MEDLINE on STN
ACCESSION NUMBER: 2003137929 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12640121
TITLE: **Manganese superoxide dismutase** -mediated gene expression in radiation-induced adaptive responses.
AUTHOR: Guo Guozheng; Yan-Sanders Yan; Lyn-Cook Beverly D; Wang Tieli; Tamae Daniel; Ogi Julie; Khaletskiy Alexander; Li Zhongkui; **Weydert Christine**; Longmate Jeffrey A; Huang Ting-Ting; Spitz Douglas R; **Oberley Larry W** ; Li Jian Jian
CORPORATE SOURCE: Radiation Biology, Division of Radiation Oncology, City of Hope National Medical Center, Duarte, California 91010, USA.
CONTRACT NUMBER: P01 CA66081 (NCI)
R01 HL51469 (NHLBI)
T32CA78586 (NCI)
SOURCE: Molecular and cellular biology, (2003 Apr) Vol. 23, No. 7, pp. 2362-78.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 26 Mar 2003
Last Updated on STN: 6 Apr 2003
Entered Medline: 4 Apr 2003

AB Antioxidant enzymes are critical in oxidative stress responses. Radioresistant variants isolated from MCF-7 human carcinoma cells following fractionated ionizing radiation (MCF+FIR cells) or overexpression of **manganese superoxide dismutase** (MCF+SOD cells) demonstrated dose-modifying factors at 10% isosurvival of 1.8 and 2.3, respectively. MCF+FIR and MCF-7 cells (exposed to single-dose radiation) demonstrated 5- to 10-fold increases in **MnSOD** activity, mRNA, and immunoreactive protein. Radioresistance in MCF+FIR and MCF+SOD cells was reduced following expression of **antisense MnSOD**. DNA microarray analysis and immunoblotting identified p21, Myc, 14-3-3 zeta, cyclin A, cyclin B1, and GADD153 as genes constitutively overexpressed (2- to 10-fold) in both MCF+FIR and MCF+SOD cells. Radiation-induced expression of these six genes was suppressed in fibroblasts from Sod2 knockout mice (-/-) as well as in MCF+FIR and MCF+SOD cells expressing **antisense MnSOD**. Inhibiting NF-kappa B transcriptional activity in MCF+FIR cells, by using mutant I kappa B alpha, inhibited radioresistance as well as reducing steady-state levels of **MnSOD**, 14-3-3 zeta, GADD153, cyclin A, and cyclin B1 mRNA. In contrast, mutant I kappa B alpha was unable to inhibit radioresistance or reduce 14-3-3 zeta, GADD153, cyclin A, and cyclin B1 mRNAs in MCF+SOD cells, where **MnSOD** overexpression was independent of NF-kappa B. These results support the hypothesis that NF-kappa B is capable of regulating the expression of **MnSOD**, which in turn is capable of increasing the expression of genes that participate in radiation-induced adaptive responses.

L23 ANSWER 2 OF 31 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:939497 SCISEARCH
THE GENUINE ARTICLE: 491RE

TITLE: Human **manganese superoxide dismutase** is specifically inhibited by **antisense** oligonucleotide **MnSOD** in human breast cancer cells.
AUTHOR: **Weydert C J (Reprint)**; Smith B B; **Oberley L W**
CORPORATE SOURCE: Univ Iowa, Iowa City, IA 52242 USA
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL CANCER RESEARCH, (NOV 2001) Vol. 7, No. 11, Supp. [S], pp. 3681S-3681S. MA 137.
ISSN: 1078-0432.
PUBLISHER: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 7 Dec 2001
Last Updated on STN: 7 Dec 2001

L23 ANSWER 3 OF 31 MEDLINE on STN
ACCESSION NUMBER: 2001170624 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11165872
TITLE: Genes regulated in human breast cancer cells overexpressing manganese-containing superoxide dismutase.
AUTHOR: Li Z; Khaletskiy A; Wang J; Wong J Y; **Oberley L W**; Li J J
CORPORATE SOURCE: Department of Radiation Research, Beckman Research Institute, City of Hope National Medical Center, 1500 Duarte Road, Duarte, CA 91010-3000, USA.
SOURCE: Free radical biology & medicine, (2001 Feb 1) Vol. 30, No. 3, pp. 260-7.
Journal code: 8709159. ISSN: 0891-5849.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 2 May 2001
Last Updated on STN: 2 May 2001
Entered Medline: 26 Apr 2001

AB The mitochondrial antioxidant enzyme manganese-containing superoxide dismutase (**MnSOD**) functions as a tumor suppressor gene. Reconstitution of **MnSOD** expression in several human cancer cell lines leads to reversion of malignancy and induces a resistant phenotype to the cytotoxic effects of TNF and hyperthermia. The signaling pathways that underlie these phenotypic changes in **MnSOD**-overexpressing cells are unknown, although alterations in the activity of several redox-sensitive transcription factors, including AP-1 and NF-kappaB, have been observed. To determine the downstream signaling molecules involved in **MnSOD**-induced cell resistant phenotype, in the present study we analyzed the expression profile of several groups of genes related to stress response, DNA repair, and apoptosis, in a human breast cancer MCF-7 cell line overexpressing **MnSOD** (MCF+SOD). Of 588 genes examined, 5 (0.85%) were up-regulated (2-42-fold), and 11 (1.9%) were down-regulated (2-33-fold) in the MCF+SOD cells compared to the parental MCF-7 cells. The five up-regulated genes were MET, GADD153, CD9, alpha-catenin and plakoglobin. The genes with the most significant down-regulation included: vascular endothelial growth factor receptor 1, TNF-alpha converting enzyme, and interleukin-1beta. GADD153 (involved in the repair of DNA double strand breaks) showed a 33-fold increase in microarray analysis and these results were confirmed by RT-PCR. To further determine the specificity in **MnSOD**-induced gene regulation, MCF+SOD cells were stably transfected with an **antisense MnSOD** sequence whose expression was controlled

by a tetracycline-inducible regulator. Expression of three up-regulated genes was measured after induction of **antisense MnSOD** expression. Interestingly, expression level of GADD153 but not MET or CD9 was reduced 24 h after **antisense MnSOD** induction. Together, these results suggest that reconstitution of **MnSOD** in tumor cells can specifically modulate the expression of down-stream effector genes. GADD153 and other elements observed in the MCF+SOD cells may play a key role in signaling the **MnSOD**-induced cell phenotypic change.

L23 ANSWER 4 OF 31 MEDLINE on STN
ACCESSION NUMBER: 2000469293 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10970696
TITLE: Suppression of manganese superoxide dismutase augments sensitivity to radiation, hyperthermia and doxorubicin in colon cancer cell lines by inducing apoptosis.
AUTHOR: Kuninaka S; Ichinose Y; Koja K; Toh Y
CORPORATE SOURCE: Clinical Research Institute, Department of Chest Surgery, Gastroenterologic Surgery, National Kyushu Cancer Center, Notame 3-1-1, Minami-ku, Fukuoka, 811-1395, Japan.
SOURCE: British journal of cancer, **(2000 Oct)** Vol. 83, No. 7, pp. 928-34.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 12 Oct 2000
Last Updated on STN: 12 Oct 2000
Entered Medline: 2 Oct 2000

AB Increased expression of manganese superoxide dismutase (Mn-SOD), one of the mitochondrial enzymes involved in the redox system, has been shown to diminish the cytotoxic effects of several anti-cancer modalities, including tumour necrosis factor-alpha, ionizing radiation, certain chemotherapeutic agents and hyperthermia. We asked if **Mn-SOD** is a potential target to augment the sensitivity of cancer cells to various anti-cancer treatments and for this we established stable **Mn-SOD antisense** RNA expressing cell clones from two **human** colon cancer cell lines, HCT116 (p53 wild-type) and DLD1 (p53 mutant-type). Suppression of Mn-SOD in HCT116 was accompanied by an increased sensitivity to radiation, hyperthermia and doxorubicin, as compared with findings in controls. The mitochondrial permeability transition, as measured by a decrease of the mitochondrial transmembrane potential was more intensely induced by radiation in HCT116 antisense clones than in the control, an event followed by a greater extent of DNA fragmentation. Apoptosis was also induced by hyperthermia more intensely in HCT116 antisense clones than in the control. On the other hand, DLD1 antisense clones did not exhibit any enhancement of sensitivity to any of these treatments. These data support the possibility that inhibition of Mn-SOD activity renders colon cancer cells with wild-type p53 susceptible to apoptosis induced by radiation, hyperthermia and selected anti-cancer drugs. Therefore, we suggest that Mn-SOD could be a target molecule to overcome the resistance to anti-cancer treatments in some colon cancer cells carrying wild-type p53.

L23 ANSWER 5 OF 31 MEDLINE on STN
ACCESSION NUMBER: 2000441795 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10924331
TITLE: The 3' UTR of **human MnSOD** mRNA hybridizes to a small cytoplasmic RNA and inhibits gene expression.
AUTHOR: Stuart J J; Egry L A; Wong G H; Kaspar R L

CORPORATE SOURCE: Department of Chemistry and Biochemistry, Brigham Young University, Provo, Utah, 84602, USA.
SOURCE: Biochemical and biophysical research communications, **(2000 Aug 11)** Vol. 274, No. 3, pp. 641-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 28 Sep 2000
Last Updated on STN: 28 Sep 2000
Entered Medline: 15 Sep 2000

AB **Human MnSOD** localizes to the mitochondria and plays a key protective role by detoxifying oxygen free radicals. The **MnSOD** mRNA 3' UTR contains a 280-bp region (Alu-like element or Alu-E) that shows high homology to **human** Alu and 7SL sequences. MnSOD 3' UTR probes hybridize to a specific cytoplasmic RNA species of approximately 300 nucleotides. This antisense RNA is most likely 7SL RNA based on its size, ubiquitousness, high levels, and lack of inducibility. Hybridization of this small RNA to the MnSOD 3' UTR may modulate posttranscriptional MnSOD gene expression. This regulation could occur by several means including inhibition of translation and mRNA destabilization. Regulation at the level of translational initiation does not seem to occur as MnSOD mRNA containing the Alu-E is efficiently bound by ribosomes. To test the role of the MnSOD 3' UTR, and in particular the Alu-E in gene expression, luciferase reporter gene constructs were made containing various regions of the MnSOD 3' UTR including the Alu-E. These constructs were transfected into human A549 lung carcinoma cells and luciferase activity was measured. Reporter constructs containing the MnSOD 3' UTR and the Alu-E repress luciferase activity. Taken together, these results suggest that naturally occurring **antisense** RNA may bind **MnSOD** mRNA and repress its expression. These results also suggest that other mRNAs containing Alu elements may be similarly repressed.

L23 ANSWER 6 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:37530 BIOSIS
DOCUMENT NUMBER: PREV200100037530
TITLE: An **antisense** oligodeoxynucleotide to **human MnSOD** effectively blocks expression and enzymatic activity.
AUTHOR(S): **Weydert, Christine J.** [Reprint author]; Smith, Benjamin B. [Reprint author]; **Oberley, Larry W.** [Reprint author]
CORPORATE SOURCE: Free Radical and Radiation Biology, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Free Radical Biology and Medicine, (**2000**) Vol. 29, No. Supplement 1, pp. S136. print.
Meeting Info.: 7th Annual Meeting of the Oxygen Society. San Diego, CA, USA. November 16-20, 2000. Oxygen Society.
CODEN: FRBMEH. ISSN: 0891-5849.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jan 2001
Last Updated on STN: 12 Feb 2002

L23 ANSWER 7 OF 31 MEDLINE on STN
ACCESSION NUMBER: 1999355000 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10428046
TITLE: Induction of the manganese superoxide dismutase gene by sphingomyelinase and ceramide.

AUTHOR: Pahan K; Dobashi K; Ghosh B; Singh I
CORPORATE SOURCE: Department of Pediatrics, Medical University of South Carolina, Charleston 29425, USA.
CONTRACT NUMBER: NS-22576 (NINDS)
NS-34741 (NINDS)
NS-37766 (NINDS)
SOURCE: Journal of neurochemistry, **(1999 Aug)** Vol. 73, No. 2, pp. 513-20.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 13 Aug 1999

AB The present study reports the effect of ceramide generated by hydrolysis of membrane sphingomyelin with bacterial sphingomyelinase (SMase) and of cell-permeable ceramide analogues on the expression of manganese superoxide dismutase (MnSOD). Incubation of the rat primary astrocytes with SMase led to a time- and dose-dependent increase in MnSOD activity. The increase in MnSOD activity was accompanied by an increase in MnSOD protein and mRNA. A similar effect on the expression of MnSOD was observed with the addition of cell-permeable ceramide analogues (C2 and C6). On the other hand, C2-dihydroceramide (N-acetylsphinganine), which lacks the functional critical double bond, was ineffective in inducing the expression of MnSOD. Nuclear run-on analysis showed that SMase and ceramide increased the rate of transcription of the MnSOD gene. Besides astrocytes, SMase was also found to induce the expression of **MnSOD** in rat mesangial cells, C6 glial cells, PC12 cells, and **human** skin fibroblasts. Markedly higher expression of mRNA, protein, and activity of **MnSOD** in skin fibroblasts from patients with Farber disease, a **human** disorder with pathognomonic accumulation of ceramide due to a deficiency of ceramidase, than in normal skin fibroblasts indicate that ceramide may act as a physiological inducer of **MnSOD** gene expression. However, stimulation of ceramide-mediated DNA fragmentation by **antisense** knockdown of **MnSOD** suggests that induction of MnSOD by ceramide is a protective response of the cell.

L23 ANSWER 8 OF 31 MEDLINE on STN
ACCESSION NUMBER: 1999120991 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9922216
TITLE: Gene transfer of mitochondrially targeted glutathione reductase protects H441 cells from t-butyl hydroperoxide-induced oxidant stresses.
AUTHOR: O'Donovan D J; Katkin J P; Tamura T; Husser R; Xu X; Smith C V; Welty S E
CORPORATE SOURCE: Department of Pediatrics, Baylor College of Medicine, Houston, Texas 77030, USA.
CONTRACT NUMBER: GM444263 (NIGMS)
HD27823 (NICHD)
HL52637 (NHLBI)
SOURCE: American journal of respiratory cell and molecular biology, **(1999 Feb)** Vol. 20, No. 2, pp. 256-63.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 24 Mar 1999
Last Updated on STN: 24 Mar 1999

Entered Medline: 11 Mar 1999

AB Increased generation of reactive oxygen species (ROS) and low levels of antioxidants may cause morbidity in premature infants on supplemental oxygen. Glutathione (GSH)-dependent antioxidant systems protect against ROS, and regenerating GSH from GSH disulfide (GSSG) by the flavoenzyme GSH reductase (GR) is essential for the optimal function of this system. Previously, we have observed enhanced resistance to t-butyl hydroperoxide (t-BuOOH) in Chinese hamster ovary cells stably transfected with a vector (leader sequence GR [LGR]) for human GR cDNA that contained a functional synthetic mitochondrial targeting signal. The present studies were designed to investigate adenovirus-mediated gene transfer of LGR to H441 cells and resistance of such cells to t-BuOOH. Adenovirus-mediated transfection of H441 cells with LGR increased total GR activities more than 11-fold (mitochondria more than 10-fold and cytosolic more than 7-fold) and protected against t-BuOOH cytotoxicity, as indicated by lower fractional release of cellular lactate dehydrogenase (LDH) than was observed in wild-type untransfected cells (CON) or in cells transfected with a control gene (**human manganese superoxide dismutase** in the **antisense** orientation [DOS]) (*LGR 6.6 +/- 1.7; DOS 16 +/- 1.8; CON 16.6 +/- 0.7% LDH release). In addition, cells transfected with LGR retained higher GSH/GSSG ratios (*LGR 66 +/- 0.4; DOS 47 +/- 1; CON 52.6 +/- 2.3) and released less GSH + GSSG to the media in response to challenge with t-BuOOH (*LGR 0.05 +/- 0.01; DOS 0.08 +/- 0.01; CON 0.07 +/- 0.01 nmol/mg of protein) than did wild-type cells or cells transfected with a control vector, indicating an enhanced ability of the LGR cells to reduce GSSG formed in response to exposure to t-BuOOH. In conclusion, adenovirus-mediated gene transfer of LGR enhanced cellular GR activities and protected H441 cells from oxidant stresses.

L23 ANSWER 9 OF 31 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 131:142751 CA

TITLE: The effect of intracellular superoxide anion radical on the expression of bcl-2, p53 and c-Ha-ras in Eca-109 esophageal carcinoma cells

AUTHOR(S): Li, Fuyang; Hui, Hongxiang; Wang, Chengji; Wang, Duoning; Mo, Jian; Li, Jianjian; **Oberley, Lary W.**

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Fourth Military Medical University, Xi'an, 710032, Peop. Rep. China

SOURCE: Journal of Medical Colleges of PLA (**1999**), 14(1), 52-56
CODEN: JMCPE6; ISSN: 1000-1948

PUBLISHER: Journal of Medical Colleges of PLA, Editorial Board

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective: To investigate the effects of intracellular superoxide anion free radical on the expression of oncogene bcl-2, p53 and c-Ha-ras. Methods: mammalian vectors expressing sense and **anti-sense human Mn-SOD** (SOD2) were constructed and transfected into Eca-109 esophageal carcinoma cells in order to change intracellular O2·- level specifically by increasing or decreasing the intracellular SOD2 level. The expression of oncogene was detected via RNA dot blotting and immunohistochem. method, and the alteration of cell cycle was observed via flow cytometry. Results: The gene expression vectors were transfected into cells. In SOD2 transfected cells, intracellular SOD2 activity increased 5-fold while SOD1 kept unchanged; intracellular O2·- was decreased over 49%; the expression of bcl-2 was down-regulated while the expression of p53 and c-Ha-ras were up-regulated. Flowcytometry assay showed the number of S-phase cells was reduced. In **anti-sense** SOD2 transfected cells, intracellular SOD2 activity was almost reduced to zero while SOD1 increased, which resulted in the increase of intracellular total SOD

activity, and the intracellular O2·- level was decreased over 32%; the expression of bcl-2, p53 and c-Ha-ras were all up-regulated, and the alteration of S-phase cells number was not obvious. Conclusions: 1. To change intracellular O2·- level via transfecting SOD2 gene into cell is feasible, but it still need further improvement. 2. Alteration of intracellular O2·- can affect the expression of bcl-2, p53 and c-Ha-ras in Eca-109 cell, and the decrease of intracellular O2·- caused by SOD2 gene transfection displayed inhibitory effect on the proliferation of Eca-109 esophageal carcinoma cells.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 31 MEDLINE on STN

ACCESSION NUMBER: 1998151391 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9482791

TITLE: **Manganese superoxide dismutase** protects nNOS neurons from NMDA and nitric oxide-mediated neurotoxicity.

AUTHOR: Gonzalez-Zulueta M; Ensz L M; Mukhina G; Lebovitz R M; Zwacka R M; Engelhardt J F; **Oberley L W**; Dawson V L; Dawson T M

CORPORATE SOURCE: Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA.

CONTRACT NUMBER: NS01578 (NINDS)
NS33142 (NINDS)
NS33277 (NINDS)

SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (1998 Mar 15) Vol. 18, No. 6, pp. 2040-55. Ref: 84
Journal code: 8102140. ISSN: 0270-6474.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199804

ENTRY DATE: Entered STN: 22 Apr 1998
Last Updated on STN: 22 Apr 1998
Entered Medline: 13 Apr 1998

AB Neuronal nitric oxide synthase (nNOS) neurons kill adjacent neurons through the action of NMDA-glutamate receptor activation, although they remain relatively resistant to the toxic effects of NMDA and NO. The molecular basis of the resistance of nNOS neurons to toxic insults is unknown. To begin to understand the molecular mechanisms of the resistance of nNOS neurons, we developed a pheochromacytoma-derived cell line (PC12) that is resistant to the toxic effects of NO. We found through serial analysis of gene expression (SAGE) that **manganese superoxide dismutase** (**MnSOD**) is enriched in the NO-resistant PC12 cell-derived line (PC12-R). **Antisense MnSOD** renders PC12-R cells sensitive to NO toxicity and increases the sensitivity to NO in the parental, NO-sensitive PC12 line (PC12-S). Adenoviral transfer of **MnSOD** protects PC12-S cells against NO toxicity. We extended these studies to cortical cultures and showed that **MnSOD** is enriched in nNOS neurons and that **antisense MnSOD** renders nNOS neurons susceptible to NMDA neurotoxicity, although it has little effect on the overall susceptibility of cortical neurons to NMDA toxicity. Overexpression of **MnSOD** provides dramatic protection against NMDA and NO toxicity in cortical cultures, but not against kainate or AMPA neurotoxicity. Furthermore, nNOS neurons from **MnSOD** -/- mice are markedly sensitive to NMDA toxicity. Adenoviral transfer of **MnSOD** to **MnSOD**-/- cultures restores resistance of nNOS neurons to NMDA toxicity. Thus, **MnSOD** is a major protective protein that appears to be essential for the resistance of nNOS neurons in cortical cultures to NMDA mediated

neurotoxicity.

L23 ANSWER 11 OF 31 MEDLINE on STN
ACCESSION NUMBER: 1998194866 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9535218
TITLE: Apoptosis caused by oxidized LDL is manganese superoxide dismutase and p53 dependent.
AUTHOR: Kinscherf R; Claus R; Wagner M; Gehrke C; Kamencic H; Hou D; Nauen O; Schmiedt W; Kovacs G; Pill J; Metz J; Deigner H P
CORPORATE SOURCE: Department of Anatomy and Cell Biology III, University of Heidelberg, Germany.
SOURCE: The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, **(1998 Apr)** Vol. 12, No. 6, pp. 461-7.
Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 30 Apr 1998
Last Updated on STN: 30 Apr 1998
Entered Medline: 17 Apr 1998
AB Oxidized low density lipoprotein (oxLDL) induces apoptosis in human macrophages (Mphi), a significant feature in atherogenesis. We found that induction of apoptosis in Mphi by oxLDL, C2-ceramide, tumor necrosis factor alpha (TNF-alpha), and hydrogen peroxide (H2O2) was associated with enhanced expression of manganese superoxide dismutase (MnSOD) and p53. Treatment of cells with p53 or **MnSOD antisense** oligonucleotides prior to stimulation with oxLDL, C2-ceramide, TNF-alpha, or H2O2 caused an inhibition of the expression of the respective protein together with a marked reduction of apoptosis. Exposure to N-acetylcysteine before treatment with oxLDL, C2-ceramide, TNF-alpha, or H2O2 reversed a decrease in cellular glutathione concentrations as well as the enhanced production of p53 and MnSOD mRNA and protein. In apoptotic macrophages of **human** atherosclerotic plaques, colocalization of **MnSOD** and p53 immunoreactivity was found. These results indicate that in oxLDL-induced apoptosis, a concomitant induction of p53 and MnSOD is critical, and suggest that it is at least in part due to an enhancement of the sphingomyelin/ceramide pathway.

L23 ANSWER 12 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:195318 CA
TITLE: Effect of intracellular superoxide anion free radical on the expression of bcl-2, p53, and c-Ha-ras in Eca-109 esophageal carcinoma cells
AUTHOR(S): Li, Fuyang; Hui, Hongxiang; Wang, Chengji; Wang, Duoning; Mo, Jian; Li, Jianjian; Oberley, Karry W.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, 4th Military Medical University, Xi'an, 710033, Peop. Rep. China
SOURCE: Disi Junyi Daxue Xuebao **(1998)**, 19(4), 365-369
CODEN: DJDXEG; ISSN: 1000-2790
PUBLISHER: Disi Junyi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB To investigate the effects of intracellular anion free radical, O2.-, on the expression of oncogene bcl-2, p53, and c-Ha-ras, the mammalian vectors expressing sense and **anti-sense human Mn-SOD** (SOD2) were constructed and transfected into Eca-109 esophageal carcinoma cells. The sense and antisense SOD2 gene expression vectors were transfected into cells and expressed. The

expression of oncogenes were detected by RNA dot blotting and immunochem. The alteration of cell cycle was observed by flowcytometry. In the sense SOD2 transfected cells, intracellular SOD2 activity increased 5 folds while SOD1 kept stable; the intracellular O2-. was decreased about 49%; the expression of bcl-2 was down-regulated and the expression of p53 and c-Ha-ras up-regulated; and the reduced number of S phase cell was observed by FCM. In anti-sense SOD2 transfected cells, intracellular SOD2 activity was almost reduced to 0 while SOD1 increased and resulted in increase of total intracellular SOD activity, and the intracellular O2-. levels was decreased about 32%, the expression of bcl-2, p53, and c-ha-ras were all up-regulated, and the change of S phase cell number was not obvious. The results suggest that the alteration of intracellular O2-. affects the expression of oncogenes and proliferation of Eca-109 cells, and the method of transfection of SOD2 gene to alter the intracellular O2-. is feasible although needs further improvement.

L23 ANSWER 13 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 129:25140 CA
TITLE: Regulation of ionizing radiation-induced apoptosis by MnSOD gene transfection
AUTHOR(S): Sun, Juan; Chen, Yuan; Zhou, Mei; Ge, Zhong-liang
CORPORATE SOURCE: Laboratory of Free Radical Medicine, First Military Medical University, Canton, 510515, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (**1998**), 30(1), 26-30
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Ionizing radiation induces the production of superoxide radicals (O.hivin.2·) which play a role in apoptosis generation. Manganese superoxide dismutase (MnSOD) is a mitochondrial antioxidant enzyme involved in scavenging O.hivin.2·. The study is designed to investigate the effect of MnSOD on ionizing radiation-induced apoptosis. The eukaryotic expression vector, pHβAPr-3p-neo, containing sense and **antisense human MnSOD** cDNA have been introduced into Chinese hamster ovary (CHO) cell resp. by gene transfection method and the **MnSOD** overexpressing cell lines have been used in this study. It was found that the cell clone overexpressing sense MnSOD increased their sensitivity. Further studies also demonstrated that alterations of mitochondrial membrane potential ($\Delta\psi m$) may play an important role in the regulatory mechanisms of MnSOD on ionizing radiation-induced apoptosis.

L23 ANSWER 14 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:341935 BIOSIS
DOCUMENT NUMBER: PREV199799641138
TITLE: Overproduction of **human Mn-superoxide dismutase** modulates tert-butylhydroperoxide(tbooH)-induced apoptosis in transformed CHO cells.
AUTHOR(S): Juan, Sun [Reprint author]; Yuan, Chen; Mei, Zhou; Zhong-Liang, Ge
CORPORATE SOURCE: Res. Lab. Free Radical Med., First Military Med. Univ., Guangzhou 510515, China
SOURCE: Medical Science Research, (**1997**) Vol. 25, No. 6, pp. 373-376.
CODEN: MSCREJ. ISSN: 0269-8951.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Aug 1997
Last Updated on STN: 11 Aug 1997
AB Manganese superoxide dismutase (MnSOD) is a nuclear encoded mitochondrial

matrix enzyme that scavenges superoxide radicals (O-2-). The sense and **antisense human MnSOD** and cDNA under the transcriptional control of a **human** beta-actin promoter were introduced into Chinese hamster ovary (CHO) cells by lipofectin transfection with recombinant plasmids containing a neomycin selectable marker. MnSOD activity increased about four-fold in cells transfected with sense MnSOD cDNA and decreased to apprx 30% in cells transfected with **antisense MnSOD** cDNA as compared with controls. Overexpression of the MnSOD gene did not alter CuZnSOD or glutathione peroxidase (GPx) activities. Upon exposure of the cells to tert-butylhydroperoxide (tbooH) (10-4 M), which can induce programmed cell death (PCD) or apoptosis, GPx activity increased mainly in cells transfected with sense MnSOD cDNA. In conclusion, the induction of apoptosis by tbooH exposure was selectively delayed in these cells expressing sense MnSOD. CHO cells expressing **antisense MnSOD** gene were more sensitive to tbooH cytotoxity than control cells. These results suggest that raised GPx activity may confer protection against tbooH-induced apoptosis in **human MnSOD** transformed cells.

L23 ANSWER 15 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:164769 BIOSIS
DOCUMENT NUMBER: PREV199799463972
TITLE: Mitochondrial alterations in CHO cells exposed to X-ray after transfecting with **human MnSOD** cDNA.
AUTHOR(S): Sun Juan, Chen Yuan [Reprint author]; Zhou Mei; Li Mingtao; Ge Zhongliang
CORPORATE SOURCE: Res. Lab. Free Radical Med., First Military Med. Univ., Guangzhou 510515, China
SOURCE: Medical Science Research, (**1997**) Vol. 25, No. 2, pp. 81-84.
CODEN: MSCREJ. ISSN: 0269-8951.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Apr 1997
Last Updated on STN: 15 Apr 1997

AB Ionising radiation induces the production of superoxide radicals(O-2-), which play an important causative role in radiation damage. Manganese superoxide dismutase (MnSOD) is a mitochondrial enzyme involved in scavenging O-2-. We have investigated the mitochondria alterations in CHO cells after transfecting with **human MnSOD** cDNA by measuring the following: (a) metabolic activity of the mitochondria by quantitative staining with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT); (b) mitochondrial membrane potential (DELTA psi-m) by a fluorescent dye rhodamine 123; and (c) cell viability by a blue exclusion test. The cSOD(+)-c1 clone, which overexpressed MnSOD after sense MnSOD cDNA transfection, showed increased mitochondrial recovery from treatment with X-ray irradiation, whereas the cSOD (-)-c1 clone transfected with **antisense MnSOD** cDNA recovered less well than normal cells from X-ray. These observations suggested that mitochondria may be the primary target of ionising radiation injury and MnSOD is important for the recovery of mitochondrial integrity and function from radiation damage.

L23 ANSWER 16 OF 31 MEDLINE on STN

ACCESSION NUMBER: 96212001 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8640453
TITLE: **Antisense manganese superoxide dismutase** mRNA inhibits the antiviral action of interferon-gamma and interferon-alpha.
AUTHOR: Raineri I; Huang T T; Epstein C J; Epstein L B
CORPORATE SOURCE: Cancer Research Institute, University of California, San

Francisco, USA.
CONTRACT NUMBER: AG 08938 (NIA)
CA 27903 (NCI)
CA 44446 (NCI)
SOURCE: Journal of interferon & cytokine research : the official journal of the International Society for Interferon and Cytokine Research, **(1996 Jan)** Vol. 16, No. 1, pp. 61-8.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 26 Jul 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 16 Jul 1996

AB Manganese superoxide dismutase (MnSOD) is induced by interferon-gamma (IFN-gamma) in various cell lines. To determine whether **MnSOD** plays a role in the antiviral action of IFN-gamma, we employed an antisense strategy to inhibit the expression of **MnSOD** in the **human** melanoma cell line, A375. Three antisense-containing clones that exhibited reduced induction of MnSOD were investigated with respect to their response to the antiviral protective effects of IFN-gamma and IFN-alpha. We observed a striking decrease in the ability of IFN-gamma to protect antisense clones from vesicular stomatitis virus infection (VSV). The IFN-alpha induced antiviral state was also impaired, but to a lesser degree than was observed with IFN-gamma. We excluded the possibility that these effects were caused by a higher sensitivity of the antisense cells to VSV itself and found that the antisense clones actually were less sensitive to VSV. Therefore, we conclude that MnSOD is involved in the establishment of the IFN-gamma-induced antiviral state and to a lesser degree in the antiviral actions of IFN-gamma.

L23 ANSWER 17 OF 31 MEDLINE on STN
ACCESSION NUMBER: 96063652 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7488155
TITLE: The use of RT-PCR to distinguish between plasmid **MnSOD** transcripts and endogenous **MnSOD** mRNA.
AUTHOR: Li J J; Domann F; **Oberley L W**
CORPORATE SOURCE: Radiation Research Laboratory, University of Iowa, Iowa City 52242, USA.
CONTRACT NUMBER: R01 CA 41267 (NCI)
SOURCE: Biochemical and biophysical research communications, (1995 Nov 13) Vol. 216, No. 2, pp. 610-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 21 Dec 1995

AB We report here a convenient RT-PCR method to distinguish plasmid human **MnSOD** cDNA transcripts from the endogenous **MnSOD** gene products without engineering the cDNA insert. When a specific **antisense** primer for the carrier vector sequence was paired with a sense primer for the human **MnSOD** cDNA in RT-PCR analysis, a unique amplicon with the expected size was generated in **MnSOD** cDNA transfected cells but not in the wild type or vector control cells. The same primers were also used in genomic DNA-PCR to demonstrate genomic incorporation of cDNA in stably transfected cells. This method is

convenient and specific in determining exogenous cDNA incorporation and expression in transfectants especially when transcripts of cDNA are difficult to separate from the endogenous mRNA by other methods.

L23 ANSWER 18 OF 31 MEDLINE on STN
ACCESSION NUMBER: 95346694 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7621245
TITLE: Role of manganese superoxide dismutase in radioprotection using gene transfer studies.
AUTHOR: Suresh A; Tung F; Moreb J; Zucali J R
CORPORATE SOURCE: Department of Medicine, College of Medicine, University of Florida, Gainesville, USA.
CONTRACT NUMBER: AI 24709 (NIAID)
AI 31918 (NIAID)
SOURCE: Cancer gene therapy, **(1994 Jun)** Vol. 1, No. 2, pp. 85-90.
Journal code: 9432230. ISSN: 0929-1903.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 11 Sep 1995
Last Updated on STN: 3 Feb 1997
Entered Medline: 31 Aug 1995

AB Overexpression of manganese superoxide dismutase (MnSOD) has been postulated as one possible mechanism of radioprotection for hematopoietic cells. In this study retroviral constructs having the **human MnSOD** gene in both the sense and antisense orientations and the Neo-R gene as a selectable marker were transfected into the **human** erythroleukemic cell line K562 and the **human** melanoma cell line A375 by electroporation. Stably transfected K562 and A375 cells selected in G418 for 3 weeks were subjected to various doses of irradiation, and cell viability was assayed using a colony assay system in semisolid medium. Results demonstrated that K562 cells transfected with **MnSOD** in the **antisense** orientation displayed increased sensitivity to irradiation compared to parental or vector-transfected K562 cells. In contrast, A375 cells transfected with the sense MnSOD gene demonstrated increased resistance to irradiation compared to parental or vector-transfected A375 cells. The expression of the MnSOD gene in these transfected cell lines correlates with the up- or down-modulation of radiosensitivity. Thus, increased MnSOD protein was seen in the A375 cells containing the sense MnSOD, whereas decreased MnSOD protein was seen in the K562 cells containing the **antisense MnSOD**. These data provide evidence for the direct role of **MnSOD** in radioprotection using **antisense** gene transfer/inhibition studies.

L23 ANSWER 19 OF 31 MEDLINE on STN
ACCESSION NUMBER: 93219435 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8464931
TITLE: Increased **manganese superoxide dismutase** expression suppresses the malignant phenotype of **human** melanoma cells.
AUTHOR: Church S L; Grant J W; Ridnour L A; **Oberley L W**; Swanson P E; Meltzer P S; Trent J M
CORPORATE SOURCE: Edward Mallinkrodt, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO 63110.
CONTRACT NUMBER: CA 41267 (NCI)
HD-00885 (NICHD)
HL-01902 (NHLBI)
+
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1993 Apr 1)** Vol. 90,

No. 7, pp. 3113-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 21 May 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 4 May 1993

AB Introduction of a normal human chromosome 6 into human melanoma cell lines results in suppression of tumorigenicity. This suggests that a gene(s) on chromosome 6 controls the malignant phenotype of human melanoma. Because antioxidants can suppress the tumor-promotion phase of carcinogenesis, and because the antioxidant enzyme **manganese superoxide dismutase** (**MnSOD**) has been localized to a region of chromosome 6 frequently lost in melanomas, we have examined the effect of transfecting sense and **antisense human MnSOD** cDNAs into melanoma cell lines. Cell lines expressing abundant (+)-sense **MnSOD**-5 cDNAs significantly altered their phenotype in culture and lost their ability to form colonies in soft agar and tumors in nude mice. In contrast, the introduction of **antisense MnSOD** or +psv2neo had no effect on melanoma tumorigenicity. These findings indicate that stable transfection of **MnSOD** cDNA into melanoma cell lines exerts a biological effect that mimics that observed after introduction of an entire **human** chromosome 6.

L23 ANSWER 20 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 119:267712 CA
TITLE: Regulation of manganese superoxide dismutase and other antioxidant genes in normal and leukemic hematopoietic cells and their relationship to cytotoxicity by tumor necrosis factor
AUTHOR(S): Kizaki, Masahiro; Sakashita, Akiko; Karmakar, Amitabha; Lin, Chi Whei; Koeffler, H. Phillip
CORPORATE SOURCE: Dep. Med., Keio Univ., Tokyo, Japan
SOURCE: Blood (**1993**), 82(4), 1142-50
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Myeloid cells are a major source of superoxide and other O metabolites. As a protective mechanism, cells express antioxidant enzymes including Mn superoxide dismutase (Mn-SOD), Cu-Zn SOD (Cu/Zn-SOD), and glutathione peroxidase (GSX-PX). Even though hematopoietic cells are a major source of oxidants, little is known of their expression of antioxidants. Seven myeloid leukemic cell lines blocked at different stages of differentiation constitutively expressed Mn-SOD, Cu/Zn-SOD, and GSX-PX RNAs. Level of Mn-SOD activities paralleled levels of Mn-SOD RNA. Terminal differentiation of native HL-60 cells to either granulocytes or macrophages did not alter levels of Mn-SOD RNA but markedly decreased cell division. Myeloid leukemic lines sensitive to cytotoxic effects of tumor necrosis factor (TNF) as well as normal peripheral blood lymphocytes and monocytes, dramatically increased their levels of MN-SOD RNA in the presence of TNF. In contrast, Cu/Zn-SOD and GSX-PX RNA levels did not increase in these same cells. TNF-resistant leukemic lines had higher constitutive levels of Mn-SOD RNA and activity; and these levels did not change in the presence of TNF. **Antisense** but not random oligonucleotides to **Mn-SOD** markedly increased the sensitivity to the inhibitory effects of TNF for both the native HL-60 (TNF-sensitive) and K562 (TNF-resistant) cell lines. The antisense oligonucleotides entered the cells and resulted in decreased levels of Mn-SOD RNA. Thus, Mn-SOD may provide protection against cytotoxicity of TNF in hematopoietic cells.

L23 ANSWER 21 OF 31 MEDLINE on STN
ACCESSION NUMBER: 93178778 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8440412
TITLE: Overexpression of mitochondrial manganese superoxide dismutase promotes the survival of tumor cells exposed to interleukin-1, tumor necrosis factor, selected anticancer drugs, and ionizing radiation.
AUTHOR: Hirose K; Longo D L; Oppenheim J J; Matsushima K
CORPORATE SOURCE: Laboratory of Molecular Immunoregulation, National Cancer Institute, Frederick Cancer Research and Development Center, Maryland 21702-1201.
SOURCE: The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, **(1993 Feb 1)** Vol. 7, No. 2, pp. 361-8.
Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 16 Apr 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 29 Mar 1993

AB Interleukin-1 (IL-1) and tumor necrosis factor (TNF) selectively induce mitochondrial manganese superoxide dismutase (MnSOD) production in various cell types. We have evaluated the capacity of tumor cells that overexpress MnSOD to recover from the cytostatic and cytotoxic effects of cytokines (IL-1 and TNF), chemotherapeutic agents, and ionizing irradiation. Clones of **human** melanoma cell line, A375, which overexpressed **MnSOD** after sense **MnSOD** cDNA transfection, showed increased recovery from treatment with cytostatic and cytotoxic doses of IL-1 alpha and TNF alpha, whereas clones of A375 cells that were transfected with **anti-sense MnSOD** cDNA recovered less well than normal cells from IL-1 alpha and TNF alpha. In addition, Chinese hamster ovary (CHO) cells transfected with sense MnSOD cDNA showed increased survival after treatment with doxorubicin, mitomycin C, and gamma (gamma) radiation in vitro. It is hypothesized that mitochondrial MnSOD, by scavenging oxygen radicals induced by cytokines, some cytotoxic drugs, and ionizing radiation, is protective and promotes the survival of cells from the lethal effects of these treatments.

L23 ANSWER 22 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:254144 BIOSIS
DOCUMENT NUMBER: PREV199395133319
TITLE: Overexpression of mitochondrial manganese superoxide dismutase promotes the survival of tumor cells exposed to interleukin-1, tumor necrosis factor, selected anticancer drugs, and ionizing radiation.
AUTHOR(S): Hirose, Kunitaka [Reprint author]; Longo, Dan L.; Oppenheim, Joost J.; Matsushima, Kouji
CORPORATE SOURCE: Biomed. Research Lab., Kureha Chem. Industry Co. Ltd., 3-26-2, Hyakunin-cho, Shinjuku-ku, Tokyo 169, Japan
SOURCE: FASEB (Federation of American Societies for Experimental Biology) Journal, (**1993**) Vol. 7, No. 2, pp. 360-368.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 May 1993
Last Updated on STN: 22 May 1993

AB Interleukin-1 (IL-1) and tumor necrosis factor (TNF) selectively induce mitochondrial manganese superoxide dismutase (MnSOD) production in various

cell types. We have evaluated the capacity of tumor cells that overexpress MnSOD to recover from the cytostatic and cytotoxic effects of cytokines (IL-1 and TNF), chemotherapeutic agents, and ionizing irradiation. Clones of **human** melanoma cell line, A375, which overexpressed **MnSOD** after sense **MnSOD** cDNA transfection, showed increased recovery from treatment with cytostatic and cytotoxic doses of IL-1-alpha and TNF-alpha, whereas clones of A375 cells that were transfected with **anti-sense MnSOD** cDNA recovered less well than normal cells from IL-1-alpha and TNF-alpha. In addition, Chinese hamster ovary (CHO) cells transfected with sense MnSOD cDNA showed increased survival after treatment with doxorubicin, mitomycin C, and gamma (gamma) radiation in vitro. It is hypothesized that mitochondrial MnSOD, by scavenging oxygen radicals induced by cytokines, some cytotoxic drugs, and ionizing radiation, is protective and promotes the survival of cells from the lethal effects of these treatments.

L23 ANSWER 23 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:316124 BIOSIS
DOCUMENT NUMBER: PREV199243016849; BR43:16849
TITLE: ESTABLISHMENT OF STABLE MELANOMA CELL LINES EXPRESSING **HUMAN MANGANESE SUPEROXIDE DISMUTASE** SENSE AND **ANTISENSE** MRNAS.
AUTHOR(S): CHURCH S L [Reprint author]; TRENT J M; GRANT J W
CORPORATE SOURCE: DEP PEDIATR, WASH UNIV SCH MED, ST LOUIS, MO, USA
SOURCE: Pediatric Research, (**1992**) Vol. 31, No. 4 PART 2, pp. 41A.
Meeting Info.: MEETING OF THE AMERICAN PEDIATRIC SOCIETY AND THE SOCIETY FOR PEDIATRIC RESEARCH, BALTIMORE, MARYLAND, USA, MAY 4-7, 1992. PEDIATR RES.
CODEN: PEREBL. ISSN: 0031-3998.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 30 Jun 1992
Last Updated on STN: 30 Jun 1992

L23 ANSWER 24 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 115:249217 CA
TITLE: Complementary DNA encoding **human** colon cancer **manganese superoxide dismutase** and the expression of its gene in **human** cells
AUTHOR(S): St. Clair, Daret K.; Holland, John C.
CORPORATE SOURCE: Bowman Gray Sch. Med., Wake Forest Univ., Winston-Salem, NC, 27103, USA
SOURCE: Cancer Research (**1991**), 51(3), 939-43
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Manganese superoxide dismutase (MnSOD) is a member of a family of metalloenzymes that catalyze the dismutation of the superoxide anion to H2O2. It has been shown that MnSOD activity in tumor cells is lower than that in their normal counterparts. To investigate the mol. basis for the reduced level of **MnSOD** activity in **human** tumor cells, the primary structure of **human MnSOD** was determined from cDNA (cDNA) isolated from a **human** colon carcinoma (HT-29) cDNA library. The sequence of the mature protein is composed of 198 amino acids preceded by a 24-amino acid leader peptide. DNA sequence anal. revealed that the translated region of the **human** tumor **MnSOD** is virtually identical to the **MnSOD** sequence isolated from normal **human** sources but exhibits differences in both the 5'- and 3'-untranslated regions. DNA blot anal. of genomic DNA

isolated from HT-29, simian virus-transformed **human** lung fibroblast (SV-40/WI-38), and parental **human** lung fibroblast (WI-38) cells showed an identical pattern of hybridization to that of **MnSOD** cDNA. RNA blot anal. revealed that tumor cells have lower levels of mnSOD mRNA. However, the half-life of the mRNA was the same (≈10 h) in tumor and normal cells. Immunol. measurement of the level of MnSOD in both normal and tumor cells also showed a reduced level of MnSOD protein in the tumor cells. These results suggest that the reduced level of **MnSOD** activity observed in **human** tumor cells is not due to a defect in the primary structure of the **MnSOD** protein, a change in the dosage of the **MnSOD** gene, or a decrease in the stability of **MnSOD** mRNA in tumor cells but rather is due to a defect or defects in the expression of the gene.

L23 ANSWER 25 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 114:158144 CA
TITLE: **Manganese superoxide dismutase**: nucleotide and deduced amino acid sequence of a cDNA encoding a new **human** transcript
AUTHOR(S): Church, Susan L.
CORPORATE SOURCE: Dep. Pediatr., St. Louis Child. Hosp., St. Louis, MO, 63110, USA
SOURCE: Biochimica et Biophysica Acta, Gene Structure and Expression (**1990**), 1087(2), 250-2
CODEN: BBGSD5; ISSN: 0167-4781
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three **human** cDNA libraries were screened with a **human manganese superoxide dismutase** (**Mn-SOD**) cDNA under moderately stringent conditions to characterize a large 4-6 kb RNA species which hybridizes to **Mn-SOD** in RNA blot analyses. A new 4.2 kb Mn-SOD cDNA clone (Mn-SOD 1) was isolated. Its long 3426 nucleotide 3'-untranslated sequence contains both of the 240 base 3'-untranslated sequences of the 1 kb Mn-SOD 4 and 5 cDNAs. This is a fully processed, cytoplasmic RNA species and raises the possibility of a role for particular 3'-untranslated sequence selection in Mn-SOD gene regulation.

L23 ANSWER 26 OF 31 MEDLINE on STN
ACCESSION NUMBER: 89376542 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2476237
TITLE: Manganous superoxide dismutase is essential for cellular resistance to cytotoxicity of tumor necrosis factor.
AUTHOR: Wong G H; Elwell J H; **Oberley L W**; Goeddel D V
CORPORATE SOURCE: Department of Molecular Biology, Genentech, Inc., South San Francisco, California 94080.
CONTRACT NUMBER: 1R01-CA41267 (NCI)
SOURCE: Cell, **(1989 Sep 8)** Vol. 58, No. 5, pp. 923-31.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 18 Oct 1989
AB Tumor necrosis factor (TNF) induces the synthesis of protein(s) that can protect cells against subsequent killing by TNF in the presence of cycloheximide. Here we demonstrate that manganous superoxide dismutase (**MnSOD**), a mitochondrial enzyme involved in the scavenging of superoxide radicals (O2-), is such a protein. Overexpression of **MnSOD** confers increased resistance to TNF plus cycloheximide on

the 293 **human** embryonic kidney cell line. Conversely, expression of **antisense MnSOD** RNA renders these cells sensitive to TNF even in the absence of cycloheximide. The TNF sensitivity of the ME-180 **human** cervical carcinoma cell line can also be modulated through expression of sense and **antisense MnSOD** RNAs. These data identify **MnSOD** as an important determinant of cellular resistance to TNF and implicate mitochondrially generated O2- as a key component of TNF-mediated tumor cell killing.

L23 ANSWER 27 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:131330 CA
TITLE: Synthesis and processing of the precursor for human mangano-superoxide dismutase
AUTHOR(S): Wispe, Jonathan R.; Clark, Jean C.; Burhans, Michael S.; Kropp, Keith E.; Korfhagen, Thomas R.; Whitsett, Jeffrey A.
CORPORATE SOURCE: Dep. Pediatr., Univ. Cincinnati, Cincinnati, OH, USA
SOURCE: Biochimica et Biophysica Acta, Protein Structure and Molecular Enzymology (**1989**), 994(1), 30-6
CODEN: BBAEDZ; ISSN: 0167-4838
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Superoxide dismutase (Mn-SOD) is encoded by nuclear chromatin, synthesized in the cytosol, and imported posttranslationally into the mitochondrial matrix. A cDNA encoding **human Mn-SOD** was isolated and sequenced. The Mn-SOD cDNA was 1001 base-pairs-long with a single open reading frame. It contained 95 base pairs of 5' untranslated sequence, and 216 base pairs of 3' untranslated sequence, followed by a short polyadenylation tract. The deduced amino acid sequence suggests a mature protein of 198 amino acids preceded by a 24-amino-acid leader peptide. A major transcript of 1000 nucleotides was identified by hybridizatio n of the cDNA with RNA isolated from human cells. Precursor **Mn-SOD** was produced by the vitro transcription of the **human Mn-SOD** cDNA followed by in vitro translation utilizing rabbit reticulocyte lysate. The primary translation product of the cDNA is a polypeptide of Mr 26,000 as determined by SDS-PAGE. When the Mr-26,000 propeptide was incubated with freshly isolated rat liver mitochondria, the peptide was proteolytically processed to a Mr-24,000 polypeptide. Proteolytic processing was accompanied by an energy-dependent import of the peptide into the isolated liver mitochondria. Mature 125I-labeled Mn-SOD, isolated from rabbit liver, was not imported in vitro into mitochondria, indicating that the energy-dependent uptake of Mn-SOD by liver mitochondria was specific for the Mn-SOD precursor.

L23 ANSWER 28 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:187326 CA
TITLE: Cloning and expression of DNA encoding **human manganese superoxide dismutase** (hMnSOD) and use of hMnSOD as anti-inflammatory agent
INVENTOR(S): Hartman, Jacob R.; Beck, Yaffa; Nimrod, Abraham
PATENT ASSIGNEE(S): Bio-Technology General Corp., USA
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 284105	A2	19880928	EP 1988-104880	19880325 <--
EP 284105	A3	19890125		

EP 284105	B1	19951115			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 01027470	A2	19890130	JP 1988-71731	19880325	<--
JP 3013896	B2	20000228			
AT 130196	E	19951215	AT 1988-104880	19880325	<--
EP 691401	A1	19960110	EP 1995-106995	19880325	<--
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 1339299	A1	19970819	CA 1988-562467	19880325	<--
IL 85876	A1	20011125	IL 1988-85876	19880325	
US 5270195	A	19931214	US 1992-912213	19920710	<--
US 6610520	B1	20030826	US 1994-299047	19940831	
US 5540911	A	19960730	US 1995-370461	19950109	<--
JP 08317789	A2	19961203	JP 1996-133970	19960528	<--
US 6361772	B1	20020326	US 1996-686466	19960725	

PRIORITY APPLN. INFO.:	IE 1986-2851	A	19861029
	IE 1986-2851	A	19861029
	US 1987-32734	A	19870327
	US 1988-161117	A	19880226
	US 1985-801090	B2	19851122
	US 1986-907051	B2	19860912
	EP 1988-104880	A3	19880325
	JP 1988-71731	A3	19880325
	US 1989-453057	A1	19891213
	US 1992-912213	A3	19920710
	US 1993-120951	B1	19930914
	US 1995-370461	A1	19950109

AB The cDNA and gene for hMnSOD are cloned and the cDNA is expressed in Escherichia coli. The recombinant hMnSOD is an antiinflammatory agent with better pharmacokinetics than CuZnSOD. Plasmid pMSE-4, containing the hMnSOD cDNA under the control of the λ P-L promoter and the cII ribosomal binding site, was constructed. E. coli transformed with this plasmid and culture in the presence of 150 ppm Mn2+ produced hMnSOD (606 units/mg soluble protein; 18.8% of the soluble protein was hMnSOD). The protein was purified by DE52 and CM52 column chromatog. The MnSOD levels in blood of rats injected s.c. with 50 mg hMnSOD/kg body weight gradually increased to a maximum of .apprx.70 μg/mL by 8 h and stayed at this level for ≥30 h. In the carrageenan paw edema model, a 24-h pretreatment with hMnSOD resulted in an anti-inflammatory response which was similar to the effect of a 2-h pretreatment with CuZnSOD.

L23 ANSWER 29 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:19206 CA
TITLE: Isolation of cDNAs encoding **human manganese superoxide dismutase**
AUTHOR(S): Heckl, Konrad
CORPORATE SOURCE: Ernst-Boehringer-Inst. Arzneimittelforsch., Vienna, A-1121, Austria
SOURCE: Nucleic Acids Research (**1988**), 16(13), 6224
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Multiple cDNAs encoding **human manganese superoxide dismutase** (EC 1.15.1.1) were isolated from a placental cDNA library by hybridization with synthetic oligonucleotide probes constructed according to the published amino acid sequence. DNA sequence anal. of the cDNAs revealed identical coding regions, but different 3'-untranslated regions. The predicted mature protein differs from the previously reported sequence and contains 198 amino acids and has a N-terminal leader sequence of 24 amino acids.

L23 ANSWER 30 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:19266 CA

TITLE: Expression of **manganese superoxide dismutase** in **human** cells
AUTHOR(S): Beck, Yaffa; Oren, Rachel; Amit, Boaz; Levanon, Avigdor; Gorecki, Marian; Hartman, Jacob R.
CORPORATE SOURCE: BioTechnol. Gen. (Israel) Ltd., Rehovot, 76326, Israel
SOURCE: UCLA Symposia on Molecular and Cellular Biology, New Series (**1988**), 82(Oxy-Radicals Mol. Biol. Pathol.), 257-69
CODEN: USMBD6; ISSN: 0735-9543
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some cDNA clones containing the entire coding region for **human Mn superoxide dismutase** (**MnSOD**) were isolated from a **human** T-lymphocyte cDNA library. Nucleotide sequence anal. of the clones suggests a mature protein of 198 amino acids preceded by a 24 amino acid prepeptide, in accordance with processing required for transport into mitochondria. Hybridization of the **human MnSOD** cDNA to poly(A)+ RNA from various sources indicates that the **MnSOD** gene is highly conserved in mammals. Two species of **human** RNA for **MnSOD** were identified, a major transcript about 1000 nucleotides (nt) long and a less abundant form of about 4000 nt. The mouse mRNA is similar in size to the **human** major transcript, whereas mRNA of bovine **MnSOD** is about 300 nt longer. No equivalent to the human minor transcript was observed in RNA from mouse and bovine sources. The abundance of both Cu/Zn and **MnSOD** mRNAs in various **human** cell lines was in the order of 10-3%. Both Cu/Zn and MnSOD mRNAs are simultaneously expressed in all cell lines and tissues examined, suggesting the importance of each of the two differentially compartmentalized enzymes for cellular survival.

L23 ANSWER 31 OF 31 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 109:87245 CA
TITLE: Isolation and characterization of complementary DNAs encoding human manganese-containing superoxide dismutase
AUTHOR(S): Ho, Ye Shih; Crapo, James D.
CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA
SOURCE: FEBS Letters (**1988**), 229(2), 256-60
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some cDNAs coding for **human** manganese-containing **superoxide dismutase** (**Mn SOD**) were isolated from a **human** liver and a dibutyryl cAMP differentiated U937 cDNA library constructed in vector λgt11. The nucleotide sequences of the insert cDNAs had an opening reading frame coding for 222 amino acid residues. The first 24 amino acids of the primarily translated polypeptide might constitute the leader peptide for transport of the precursors to the mitochondria. Differentiation of the U937 cells with dibutyryl cAMP resulted in a 70% decrease in Mn SOD mRNA. The amino acid sequences of the mature **Mn SODs** of **human**, rat, and mouse are highly conserved, while the sequences of the leader peptides of these species are moderately conserved.

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L28 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 96090132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7483847
TITLE: Characterization of Na+/H(+)-antiporter gene closely related to the salt-tolerance of yeast Zygosaccharomyces rouxii.
AUTHOR: Watanabe Y; Miwa S; Tamai Y
CORPORATE SOURCE: Department of Biological Resources, Faculty of Agriculture, Ehime University, Japan.
SOURCE: Yeast (Chichester, England), **(1995 Jul)** Vol. 11, No. 9, pp. 829-38.
Journal code: 8607637. ISSN: 0749-503X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D43629
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 29 Jan 1999
Entered Medline: 28 Dec 1995

AB In order to clarify the relationship between salt-tolerance of Zygosaccharomyces rouxii and the function of Na+/H(+)-antiporter, a gene was isolated from Z. rouxii which exhibited homology to the Na+/H(+)-antiporter gene (**sod2**) from Schizosaccharomyces pombe. This newly isolated gene (Z-**SOD2**) encoded a product of 791 amino acids, which was larger than the product encoded by its Sz. pombe homologue. The predicted amino-acid sequence of Z-Sod2p was highly homologous to that of the Sz. pombe protein, but included an extra-hydrophilic stretch in the C-terminal region. The expression of Z-**SOD2** was constitutive and independent of NaCl-shock. Z-**SOD2**-disruptants of Z. rouxii did not grow in media supplemented with 3 M-NaCl, but grew well in the presence of 50% sorbitol, indicating that the function of Z-**SOD2** was closely related to the salt-tolerance of Z. rouxii. Several genes are also compared and discussed in relation to the salt-tolerance of Z. rouxii.

L28 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 92406726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1526970
TITLE: Yeast lacking superoxide dismutase. Isolation of genetic suppressors.
AUTHOR: Liu X F; Elashvili I; Gralla E B; Valentine J S; Lapinskas P; Culotta V C
CORPORATE SOURCE: Department of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21205.
CONTRACT NUMBER: ES 07141 (NIEHS)
GM 28222 (NIGMS)
P03 ES 03819 (NIEHS)
SOURCE: The Journal of biological chemistry, **(1992 Sep 15)** Vol. 267, No. 26, pp. 18298-302.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 6 Nov 1992
Last Updated on STN: 6 Nov 1992
Entered Medline: 19 Oct 1992

AB Null mutants of superoxide dismutase (SOD) in Saccharomyces cerevisiae are associated with a number of biochemical defects. In addition to being

hypersensitive to oxygen toxicity, strains containing deletions in both the SOD1 (encoding Cu/Zn-SOD) and **SOD2** (encoding Mn-SOD) genes are defective in sporulation, are associated with a high mutation rate, and are unable to biosynthesize lysine and methionine. The sod-linked defect in lysine metabolism was explored in detail and was found to occur at an early step in lysine biosynthesis, evidently at the level of the alpha-amino adipate transaminase. To better understand the role of SOD in cell metabolism, our laboratory has isolated yeast suppressors that have bypassed the SOD defect ("bsd" strains), that is, S. cerevisiae cells lacking SOD, yet resistant to oxygen toxicity. Two **nuclear** bsd **complementation** groups have been identified, and both suppress a variety of biological defects associated with sod1 and **sod2** null mutants. These results demonstrate that a single gene mutation can alleviate the requirement for SOD in cell growth. Both bsd complementation groups are unable to utilize many non-fermentable carbon sources, suggesting a possible suppressor-linked defect in electron transport.

L28 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:266775 BIOSIS
DOCUMENT NUMBER: PREV199598281075
TITLE: Generation and characterization of a human chromosome 6-specific hncDNA library from a somatic cell hybrid.
AUTHOR(S): Piontek, K.; Mueller, H. W.; Fischer, U.; Goettert, E.; Batzer, M. A.; Meltzer, P. S.; Trent, J. M.; Meese, Eckart [Reprint author]
CORPORATE SOURCE: Dep. Human Genetics, Bau 68, Med. Sch., Univ. Hosp., Univ. Saar, 66421 Homburg/Saar, Germany
SOURCE: Cytogenetics and Cell Genetics, (**1995**) Vol. 69, No. 3-4, pp. 273-278.
CODEN: CGCGBR. ISSN: 0301-0171.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 1995
Last Updated on STN: 26 Jun 1995

AB Chromosome specific cDNA libraries are a useful source of candidate genes for disorders which have been linked to particular chromosomes. Here, we report the generation of a cDNA library made from a somatic cell hybrid retaining chromosome 6 as its only human component. In order to ascertain the chromosomal location of cDNAs the library was amplified by inter-Alu-PCR and used as probe for competitive in situ suppression (CISS). To identify human specific cDNA clones the library was screened with PD39, a highly human specific Alu consensus probe. Out of 350,000 clones 360 were found to hybridize with PD39. Nucleotide sequences were determined for 40 clones with inserts larger than 500 basepairs (bp) and a sequence comparison was performed at the National Center for Biotechnology Information using BLASTN. One clone was shown to be identical to Manganese Superoxide Dismutase (MnSOD/**SOD2**) which has previously been assigned to chromosome 6q25. Localization of 11 clones was determined using PCR and clone-specific primer pairs on a hybrid mapping panel DNA set. Two PCR-localized clones and five additional clones were localized by fluorescence in situ hybridization. Transcripts for five clones were identified by RT-PCR. The generation of chromosome 6-specific hncDNAs from a somatic cell hybrid should aid in the identification of disease-associated genes localized on this chromosome.

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